Metabolic syndrome (MetS) is a useful tool for identifying individuals at risk for type 2 diabetes and coronary heart disease (CHD). The syndrome has confused practitioners because of differences in definition, though definitions have come closer together over the years; however, the principles are clear: persons who have glucose intolerance, blood pressure elevation, dyslipidemia, and central obesity are at increased risk for type 2 diabetes mellitus and CHD. Identifying the presence in a given patient of the items in the cluster serves as a warning that risk of disease is increased, and should stimulate the practitioner to institute preventive measures early, with lifestyle change initially, and pharmacotherapy subsequently, as indicated by any continued risk factor presence.

Controversy in Diagnosis and Management of the Metabolic Syndrome

Far more work remains to be done to unravel the tangled web of pathophysiology responsible for the metabolic syndrome. This article addresses several aspects of the current controversy surrounding the metabolic syndrome: (1) definition of the metabolic
syndrome; (2) evidence for and against the use of the metabolic syndrome as a cardiovascular disease risk predictor; (3) evidence as to underlying pathophysiology; and (4) evidence for treatment of the metabolic syndrome (as opposed to components of the syndrome) in a risk reduction strategy to prevent type 2 diabetes mellitus or cardiovascular disease.

Insulin Resistance as the Underlying Cause for the Metabolic Syndrome

Danielle Lann and Derek LeRoith

Classically, the metabolic syndrome is characterized as group of pathologies including visceral obesity, hypertension, dyslipidemia, and impaired glucose tolerance. It is now realized that insulin resistance plays a principal role in initiating and perpetuating the pathologic manifestations of the metabolic syndrome. A more in-depth understanding of the basic pathophyslogic mechanisms underlying insulin resistance may aid clinicians in treating and possibly delaying or even preventing the onset of the metabolic syndrome and its complications. This article outlines how abnormal insulin signaling and secretion, impaired glucose disposal, lipotoxicity, and proinflammatory cytokines exacerbate insulin resistance and result in the perturbations of the metabolic syndrome.

America on the Move

Victoria A. Catenacci and Holly R. Wyatt

The population is gaining weight, despite our best current obesity education and awareness efforts. America on the Move, a nonprofit public health initiative, was founded to promote small achievable behavioral changes to help stop weight gain, starting with (1) eating 100 kcal less per day and (2) increasing lifestyle activity by 2000 steps per day. These two small changes could stop weight gain and prevent overweight and obesity in many, if not most patients. America on the Move materials and tools to implement, support and sustain these behaviors are available free of charge for individuals, schools, groups, communities, and worksites via a Web based portal. A physician tool kit is also available for health care providers to facilitate these changes in clinical practices.

Prevention of Diabetes Development in Those with the Metabolic Syndrome

Traci Tupper and Geetha Gopalakrishnan

Metabolic syndrome is characterized by abnormal glucose levels, central obesity, hypertension, elevated triglycerides, and low HDL cholesterol. This article reviews available data regarding the impact of lifestyle modification and drug therapies on the progression to diabetes in high risk individuals, such as those with hypertension, dyslipidemia, obesity, and prediabetes. Lifestyle and pharmaco-
logical interventions may alter metabolic parameters and impact progression to diabetes. However, the cost-effectiveness of these interventions are unclear.

Metabolic Syndrome and Type 2 Diabetes: Can We Stop the Weight Gain with Diabetes? 1107
Denise Joffe and Robert T. Yanagisawa

Many patients with type 2 diabetes also have the metabolic syndrome with its cardinal features of central adiposity, insulin resistance, dyslipidemia, and hypertension. Although there is strong evidence for the importance of tight glycemic control in minimizing the microvascular complications of diabetes, many of the current therapies used for optimizing glycemic control also cause weight gain. With this treatment-induced weight gain, there is a risk of worsening the patient’s insulin resistance. Physicians need to be aware of this vicious cycle in their overweight type 2 diabetic patients. This article reviews the strategies currently available to achieve glycemic control while at the same time minimizing weight gain and the associated complications.

Nonalcoholic Fatty Liver Disease as a Complication of Insulin Resistance 1125
Manal F. Abdelmalek and Anna Mae Diehl

Nonalcoholic fatty liver disease (NAFLD) refers to a spectrum of liver damage ranging from simple steatosis to nonalcoholic steatohepatitis, advanced fibrosis, and rarely, progression to cirrhosis. The pathogenesis of NAFLD is thought to be related to insulin resistance and oxidant stress. Truncal obesity, dyslipidemia, hypertension, and hyperglycemia are strongly associated with NAFLD; therefore, management of NAFLD entails identification and treatment of metabolic risk factors, improving insulin sensitivity, and increasing antioxidant defenses in the liver. This article briefly summarizes advances in our understanding of the relationship between NAFLD and the insulin resistance (metabolic) syndrome, its prevalence, natural history, and treatment.

Obesity and the Polycystic Ovary Syndrome 1151
Michael Magnotti and Walter Futterweit

Polycystic ovarian syndrome (PCOS) is extremely common among reproductive-aged women, but often goes undiagnosed. PCOS is associated with the metabolic syndrome and carries a greatly increased risk of impaired glucose tolerance and type 2 diabetes mellitus, and cardiovascular risks. Treatment of PCOS may provide relief of cosmetic problems and depression by improving patient self-esteem. In addition, because of its association with the metabolic syndrome, type 2 diabetes mellitus, and cardiovascular disease, its recognition and treatment can potentially be life saving.
This article reviews the impact, pathophysiology, and associated risks of obesity and the metabolic syndrome in PCOS.

Cardiovascular Morbidity and Mortality of the Metabolic Syndrome

Kotaro Obunai, Sonal Jani, and George D. Dangas

Cardiovascular disease remains the single leading cause of morbidity and mortality in the United States. The metabolic syndrome has received increased attention in recent years, partly because of the growing prevalence of obesity and its association with cardiovascular disease. This article reviews current evidence from longitudinal observational studies that evaluated the impact of metabolic syndrome on cardiovascular morbidity and mortality in various population subsets. The approach to cardiovascular risk assessment in individuals who have multiple risk factors and the clinical implications of diagnosing the metabolic syndrome are also discussed.

Treatment of the Dyslipidemia of Insulin Resistance

Donald A. Smith

The increase in ischemic cardiovascular mortality and morbidity in persons with insulin resistance has been adequately documented elsewhere in this issue. Some of the most important risk factors for this increased mortality and morbidity are the lipid abnormalities, which form two out of five criteria for defining the metabolic syndrome, a definition focusing on risk factors for ischemic cardiovascular disease. This article explores the description, pathophysiology, and treatment of these atherogenic lipid abnormalities.

Treatment of Hypertension and Other Cardiovascular Risk Factors in Patients with Metabolic Syndrome

Takeki Suzuki and Shunichi Homma

Metabolic syndrome (MetS), a concurrence of hypertension, abdominal obesity, impaired fasting glucose, and dyslipidemia, has been shown to be a risk factor for cardiovascular disease. Insulin resistance has been thought to be one of the pathophysiologies of the syndrome. Reduction of the underlying causes of MetS, such as obesity, physical inactivity, and atherogenic diet, is first-line therapy. Treatment of hypertension and other cardiometabolic risk factors of MetS is also required. This article reviews the treatment of the metabolic syndrome with a focus on the importance of lifestyle changes and treatment of hypertension.
Medical Therapy for Obesity—Current Status and Future Hopes

George A. Bray

In accepting any new drug for the treatment of obesity, the safety profile must make it acceptable for almost everyone. Criteria for selecting treatments involve evaluating the risks to the individual from obesity and balancing that against any possible problems with the treatment. Obesity is a chronic disease that has many causes. Cure is rare and treatment is thus aimed at palliation, that is, producing and maintaining weight loss. Wherever the primary site of action may be, however, the net effect must be a reduction in food intake or an increase in energy expenditure.

Bariatric Surgery for Morbid Obesity—A Cure for Metabolic Syndrome?

Subhash Kini, Daniel M. Herron, and Robert T. Yanagisawa

At present there is no single medication that targets the metabolic syndrome directly. Bariatric surgery, a treatment option for morbidly obese individuals who fail medical therapy, has been shown to be very effective in treating multiple aspects of the metabolic syndrome. The decrease in insulin resistance is because of significant weight loss and by enhancing secretion of gut hormones such as glucagon-like peptide-1 (GLP-1).

Index